

Amendments to the Claims

1.-9. (Canceled)

10. (Previously presented) A method for treating sexual arousal disorder comprising:
administering to a female subject in need thereof, an effective amount of an estrogen agonist / antagonist, and further comprising co-administrering a cyclic guanosine 3',5'-monophosphate elevator.

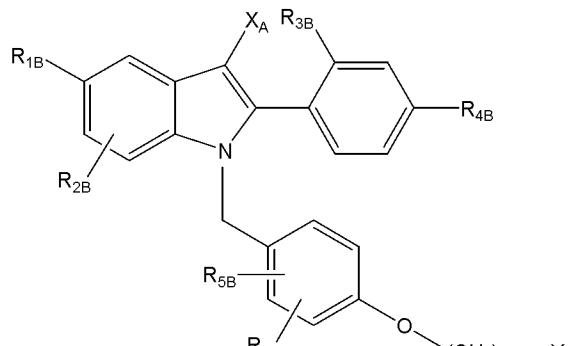
11. (Previously presented) The method of claim 10 wherein said cyclic guanosine 3',5'-monophosphate elevator is a PDE_V phosphodiesterase inhibitor.

12. (Previously presented) The method of claim 11 wherein the PDE_V phosphodiesterase inhibitor is 1-[[3-(6,7-dihydro-1-methyl-7-oxo-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-5-yl)-4-ethoxy-phenyl]sufonyl]-4-methylpiperazine citrate salt.

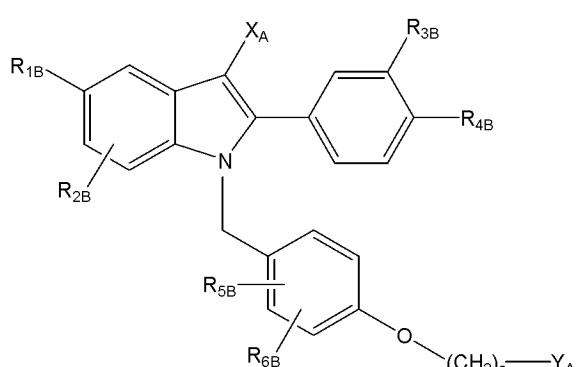
Claims 13.-39. (canceled)

40. (Currently amended) The method of claim 4 10 wherein said estrogen agonist / antagonist is selected from the group consisting of tamoxifen, 4-hydroxy tamoxifen, raloxifene, toremifene, centchroman, idoxifene, 6-(4-hydroxy-phenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-benzyl]-naphthalen-2-ol, {4-[2-(2-aza-bicyclo[2.2.1]hept-2-yl)-ethoxy]-phenyl}-[6-hydroxy-2-(4-hydroxy-phenyl)-benzo[b]thiophen-3-yl]-methanone, EM-652, EM-800, GW 5638, GW 7604, or an optical or geometric isomer thereof; a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt, or prodrug thereof.

41. (Currently amended) The method of claim 4 10 wherein said estrogen agonist / antagonist is a compound selected from the formulas V or VI:



(V)



(VI)

wherein:

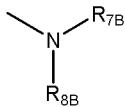
R_{1B} is selected from H, OH, -O-C(O)-C₁-C₁₂ alkyl (straight chain or branched), -O-C₁-C₁₂ alkyl (straight chain or branched or cyclic), or halogens or C₁-C₄ halogenated ethers,

R_{2B}, R_{3B}, R_{4B}, R_{5B}, and R_{6B} are independently selected from H, OH, -O-C(O)-C₁-C₁₂ (straight chain or branched), -O-C₁-C₁₂ (straight chain or branched or cyclic), halogens, or C₁-C₄ halogenated ethers, cyano, C₁-C₆ alkyl (straight chain or branched), or trifluoromethyl, with the proviso that, when R_{1B} is H, R_{2B} is not OH;

X_A is selected from H, C₁-C₆ alkyl, cyano, nitro, trifluoromethyl, and halogen;

s is 2 or 3;

Y_A is the moiety:

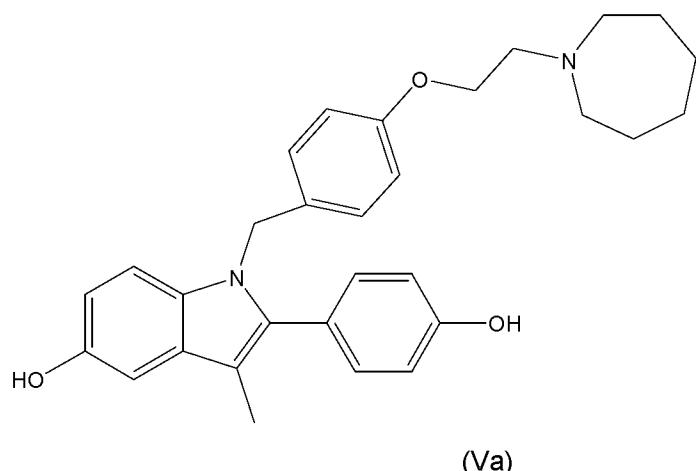


wherein:

- a) R_{7B} and R_{8B} are independently selected from the group of H, C₁-C₆ alkyl, or phenyl optionally substituted by CN, C₁-C₆ alkyl (straight chain or branched), C₁-C₆ alkoxy (straight chain or branched), halogen, -OH, -CF₃, or -OCF₃; or
- b) R_{7B} and R_{8B} are concatenated to form a five-membered saturated heterocycle containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, C₁-C₄ alkyl, trihalomethyl, C₁-C₄ alkoxy, trihalomethoxy, C₁-C₄ acyloxy, C₁-C₄ alkylthio, C₁-C₄ alkylsulfinyl, C₁-C₄ alkylsulfonyl, hydroxy (C₁-C₄)alkyl, -CO₂H, -CN, -CONHR_{1B}, -NH₂, -NH(C₁-C₄ alkyl), -N(C₁-C₄ alkyl)₂, -NHSO₂R_{1B}, -NHCOR_{1B}, -NO₂, or phenyl optionally substituted with 1-3 (C₁-C₄)alkyl; or
- c) R_{7B} and R_{8B} are concatenated to form a six-membered saturated heterocycle containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, C₁-C₄ alkyl, trihalomethyl, C₁-C₄ alkoxy, trihalomethoxy, C₁-C₄ acyloxy, C₁-C₄ alkylthio, C₁-C₄ alkylsulfinyl, C₁-C₄ alkylsulfonyl, hydroxy (C₁-C₄)alkyl, -CO₂H, -CN, -CONHR_{1B}, -NH₂, -NH(C₁-C₄ alkyl), -N(C₁-C₄ alkyl)₂, -NHSO₂R_{1B}, -NHCOR_{1B}, -NO₂, or phenyl optionally substituted with 1-3 (C₁-C₄)alkyl; or
- d) R_{7B} and R_{8B} are concatenated to form a seven-membered saturated heterocycle containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, C₁-C₄ alkyl, trihalomethyl, C₁-C₄ alkoxy, trihalomethoxy, C₁-C₄ acyloxy, C₁-C₄ alkylthio, C₁-C₄ alkylsulfinyl, C₁-C₄ alkylsulfonyl, hydroxy (C₁-C₄)alkyl, -CO₂H, -CN, -CONHR_{1B}, -NH₂, -NH(C₁-C₄ alkyl), -N(C₁-C₄ alkyl)₂, -NHSO₂R_{1B}, -NHCOR_{1B}, -NO₂, or phenyl optionally substituted with 1-3 (C₁-C₄)alkyl; or

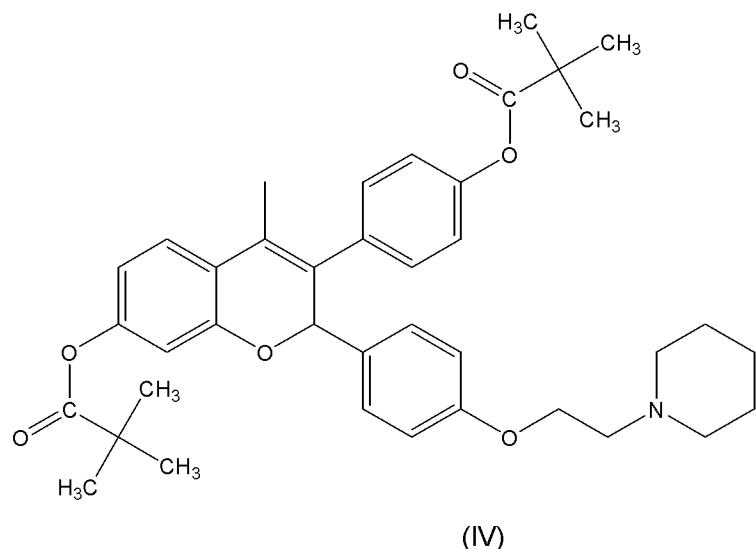
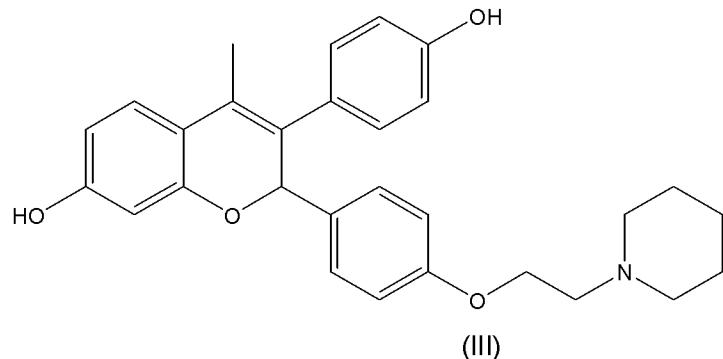
- e) R_{7B} and R_{8B} are concatenated to form an eight-membered saturated heterocycle containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, C₁-C₄ alkyl, trihalomethyl, C₁-C₄ alkoxy, trihalomethoxy, C₁-C₄ acyloxy, C₁-C₄ alkylthio, C₁-C₄ alkylsulfinyl, C₁-C₄ alkylsulfonyl, hydroxy (C₁-C₄)alkyl, -CO₂H, -CN, -CONHR₁, -NH₂, -NH(C₁-C₄ alkyl), -N(C₁-C₄ alkyl)₂, -NHSO₂R_{1B}, -NHCOR_{1B}, -NO₂, or phenyl optionally substituted with 1-3 (C₁-C₄)alkyl; or
- f) R_{7B} and R_{8B} are concatenated to form a saturated bicyclic heterocycle containing from 6-12 carbon atoms either bridged or fused and containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, C₁-C₄ alkyl, trihalomethyl, C₁-C₄ alkoxy, trihalomethoxy, C₁-C₄ acyloxy, C₁-C₄ alkylthio, C₁-C₄ alkylsulfinyl, C₁-C₄ alkylsulfonyl, hydroxy (C₁-C₄)alkyl, -CO₂H, -CN, -CONHR_{1B}, -NH₂, -NH(C₁-C₄ alkyl), -N(C₁-C₄ alkyl)₂, -NHSO₂R_{1B}, -NHCOR_{1B}, -NO₂, or phenyl optionally substituted with 1-3 (C₁-C₄) alkyl; ~~or an optical or geometric isomer thereof;~~ or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt or prodrug thereof.

42. (Previously presented) The method of claim 41 wherein said estrogen agonist / antagonist is the compound, TSE-424, of formula Va below:



or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt or prodrug thereof.

43. (Currently amended) The method of claim 4 10 wherein said estrogen agonist / antagonist is EM-652 of formula III below or is EM-800 of formula IV below:



or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt or prodrug thereof.

44. – 45. (Canceled)

46. (Currently amended) A method for treating sexual arousal disorder comprising: administering to a female subject in need thereof, an effective amount of (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol or an optical or geometric isomer thereof; a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt, or a prodrug thereof and further comprising co-

administering an effective amount of a cyclic guanosine 3',5'-monophosphate elevator.

47. (Previously presented) The method of claim 46 wherein the cyclic guanosine 3',5'-monophosphate elevator is a PDE_V phosphodiesterase inhibitor.

48. (Previously presented) The method of claim 47 wherein the PDE_V phosphodiesterase inhibitor is 1-[[3-(6,7-dihydro-1-methyl-7-oxo-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-5-yl)-4-ethoxy-phenyl]sufonyl]-4-methylpiperazine citrate salt.

49. (canceled)

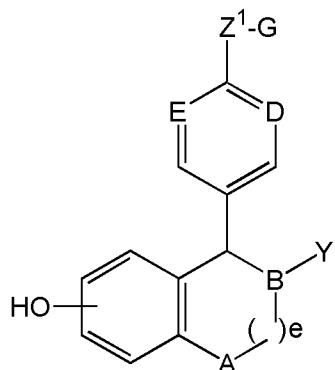
50. (Currently amended) The method of claim 46, 47 or 48 wherein (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol, D-tartrate salt is administered 45 wherein the female subject is postmenopausal.

51. (Currently amended) The method of claim 45 48 wherein the female subject is pre-menopausal.

52. (Previously presented) The method of claim 46 wherein the female subject is postmenopausal.

53. (Previously presented) The method of claim 46 wherein the female subject is pre-menopausal.

54. (new) The method of claim 10 wherein the estrogen agonist/antagonist is a compound of formula (I):



(I)

wherein:

A is selected from CH₂ and NR;

B, D and E are independently selected from CH and N;

Y is

(a) phenyl, optionally substituted with 1-3 substituents

independently selected from R⁴;

(b) naphthyl, optionally substituted with 1-3 substituents

independently selected from R⁴;

(c) C₃-C₈ cycloalkyl, optionally substituted with 1-2 substituents

independently selected from R⁴;

(d) C₃-C₈ cycloalkenyl, optionally substituted with 1-2 substituents

independently selected from R⁴;

(e) a five membered heterocycle containing up to two heteroatoms

selected from the group consisting of -O-, -NR²- and -S(O)_n-, optionally substituted

with 1-3 substituents independently selected from R⁴;

(f) a six membered heterocycle containing up to two heteroatoms

selected from the group consisting of -O-, -NR²- and -S(O)_n- optionally substituted

with 1-3 substituents independently selected from R⁴; or

(g) a bicyclic ring system consisting of a five or six membered

heterocyclic ring fused to a phenyl ring, said heterocyclic ring containing up to two

heteroatoms selected from the group consisting of -O-, -NR²- and -S(O)_n-, optionally

substituted with 1-3 substituents independently selected from R⁴;

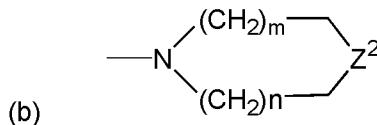
Z¹ is

(a) -(CH₂)_p W(CH₂)_q-;

- (b) $-\text{O}(\text{CH}_2)_p \text{CR}^5\text{R}^6-$;
- (c) $-\text{O}(\text{CH}_2)_p \text{W}(\text{CH}_2)_q-$;
- (d) $-\text{OCHR}^2\text{CHR}^3-$; or
- (e) $-\text{SCHR}^2\text{CHR}^3-$;

G is

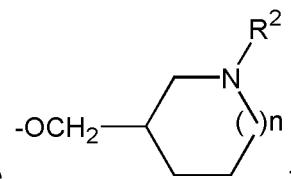
- (a) $-\text{NR}^7\text{R}^8-$;



wherein n is 0, 1 or 2; m is 1, 2 or 3; Z² is -NH-, -O-, -S-, or -CH₂-;

optionally fused on adjacent carbon atoms with one or two phenyl rings and,
optionally independently substituted on carbon with one to three substituents and,
optionally, independently on nitrogen with a chemically suitable substituent selected
from R⁴; or

(c) a bicyclic amine containing five to twelve carbon atoms, either
bridged or fused and optionally substituted with 1-3 substituents independently
selected from R⁴; or

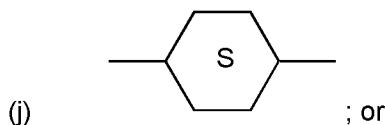


Z¹ and G in combination may be

W is

- (a) $-\text{CH}_2-$;
- (b) $-\text{CH}=\text{CH}-$;
- (c) $-\text{O}-$;
- (d) $-\text{NR}^2-$;
- (e) $-\text{S}(\text{O})_n-$;

- (f) $\begin{array}{c} \text{O} \\ \parallel \\ \text{---C---} \end{array}$;
- (g) $-\text{CR}^2(\text{OH})-$;
- (h) $-\text{CONR}^2-$;
- (i) $-\text{NR}^2\text{CO}-$;



(k) -C≡C-;

R is hydrogen or C₁-C₆ alkyl;

R² and R³ are independently

- (a) hydrogen; or
- (b) C₁-C₄ alkyl;

R⁴ is

- (a) hydrogen;
- (b) halogen;
- (c) C₁-C₆ alkyl;
- (d) C₁-C₄ alkoxy;
- (e) C₁-C₄ acyloxy;
- (f) C₁-C₄ alkylthio;
- (g) C₁-C₄ alkylsulfinyl;
- (h) C₁-C₄ alkylsulfonyl;
- (i) hydroxy (C₁-C₄)alkyl;
- (j) aryl (C₁-C₄)alkyl;
- (k) -CO₂H;
- (l) -CN;
- (m) -CONHOR;
- (n) -SO₂NHR;
- (o) -NH₂;
- (p) C₁-C₄ alkylamino;
- (q) C₁-C₄ dialkylamino;
- (r) -NHSO₂R;
- (s) -NO₂;
- (t) -aryl; or
- (u) -OH;

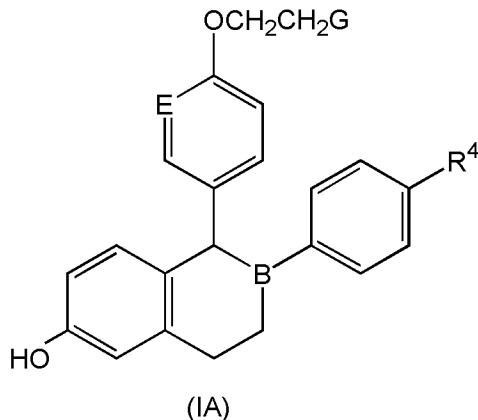
R⁵ and R⁶ are independently C₁-C₈ alkyl or together form a C₃-C₁₀ carbocyclic ring;

R⁷ and R⁸ are independently

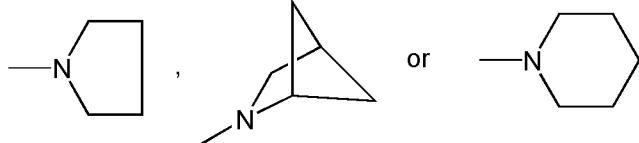
- (a) phenyl;

(b) a C₃-C₁₀ carbocyclic ring, saturated or unsaturated;
(c) a C₃-C₁₀ heterocyclic ring containing up to two heteroatoms, selected from -O-, -N- and -S-;
(d) H;
(e) C₁-C₆ alkyl; or
(f) form a 3 to 8 membered nitrogen containing ring with R⁵ or R⁶; R⁷ and R⁸ in either linear or ring form may optionally be substituted with up to three substituents independently selected from C₁-C₆ alkyl, halogen, alkoxy, hydroxy and carboxy;
a ring formed by R⁷ and R⁸ may be optionally fused to a phenyl ring;
e is 0, 1 or 2;
m is 1, 2 or 3;
n is 0, 1 or 2;
p is 0, 1, 2 or 3;
q is 0, 1, 2 or 3;
or an optical or geometric isomer thereof; or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt or prodrug thereof.

55. (new) The method of claim 54 wherein said estrogen agonist / antagonist is a compound of formula (IA):



wherein G is



R⁴ is H, OH, F, or Cl; and B and E are independently selected from CH and N or an optical or geometric isomer thereof; or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt, or a prodrug thereof.